

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
7 October 2004 (07.10.2004)

PCT

(10) International Publication Number
WO 2004/084819 A3

(51) International Patent Classification⁷: **A61K 9/16**

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number:
PCT/US2004/008399

(22) International Filing Date: 19 March 2004 (19.03.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/455,590 19 March 2003 (19.03.2003) US

(71) Applicant (for all designated States except US): **UNIVERSITY OF KENTUCKY RESEARCH FOUNDATION** [US/US]; 442 Bowman Hall, Lexington, KY 40506-0058 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DELUCA, Patrick** [US/US]; 3292 Nantucket Drive, Lexington, KY 40502 (US). **JIANG, Ge** [CN/US]; 3204-11 Stonethrow Lane, Durham, NC 27713 (US). **WOO, Byung** [KR/US]; 1329 Lunt Court, Schaumburg, IL 60193 (US).

(74) Agents: **REA, Teresa, Stanek et al.**; Burns, Doane, Swecker & Mathis, LLP, P.O. Box 1404, Alexandria, VA 22313-1404 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

Published:

— with international search report

(88) Date of publication of the international search report:
29 December 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **POLY(ACRYLOYL-HYDROXYETHYL STARCH)-PLGA COMPOSITE MICROSPHERES**

(57) Abstract: The present invention relates to a composite microsphere system comprising poly(D,L-lactide-co-glycolide) (PLGA), poly(acryloyl hydroxyethyl starch) (AChES), and a pharmaceutically effective amount of a biologically active compound. The active compound may be, for example, an insulin, an interferon, a luteinizing hormone-releasing hormone (LHRH) analog, a somatostatin and/or derivatives thereof, a calcitonin, a parathyroid hormone (PTH), a bone morphogenic protein (BMP), an erythropoietin (EPO), an epidermal growth factor (EGF) or a growth hormone. This invention also relates to methods of using the composite microspheres, and methods of preparing same.

WO 2004/084819 A3

INTERNATIONAL SEARCH REPORT

International app. No.

PCT/US04/08399

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 9/16

US CL : 424/490

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/490

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,160,745 A (DELUCA et al.) 03 November 1992 (03.11.1992), see entire document.	1-15
A	US 5,922,340 A (BERDE et al.) 13 July 1999 (13.07.1999), see entire document.	1-15

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

25 August 2004 (25.08.2004)

Date of mailing of the international search report

22 SEP 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

BLESSING FUBARA

Telephone No. (571) 272-1600